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A practical route to 3,6-dideoxyhexoses

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Abstract

Novel, readily scaled and practical routes for the synthesis of 3,6-dideoxy-D-*xylo*-hexose and 3,6-dideoxy-D-*ribo*-hexose and their corresponding glycosyl donors are presented. The method uses a 1,2-*O*-propylidene acetal to protect the monosaccharides, glucose and galactose, thereby permitting not only easy modification at both 3 and 6 positions, but also the opportunity to readily place different protecting groups on OH-2 and OH-4.

1. Introduction

The 3,6-dideoxyhexoses are found almost exclusively in the O-antigen segment of the lipopolysaccharide (LPS) molecule, that is located in the outer cell wall of gram-negative bacteria.[1–4] Their presence as terminal branching residues coincides with an immunodominant role as the principal structural element recognised by the antibodies of anti-sera used to type bacterial serogroups.[4] For example, paratose (3,6-dideoxy-D-*ribo*-hexopyranose **1**), and abequose (3,6-dideoxy-D-*xylo*-hexopyranose **2**) (Fig. 1) are both expressed in the cell wall LPS of *Salmonella*. In the lipopolysaccharide O-antigen of serogroup A *Salmonella*, paratose is α-linked to a common linear Man-Rha-Gal sequence, while in the O-antigen of serogroup B *Salmonella*, abequose is α-linked to the same Man-Rha-Gal sequence.[4]

A number of methods have appeared in the literature for the preparation of these 3,6-dideoxy sugars.[5–13] For paratose the direct 3,6-dihalogenation of methyl α-D-glucopyranoside, followed by hydrogenation in the presence of base, is the most efficient method to prepare paratose, while reduction of methyl 3,4-anhydro-6-*O*-*p*-toluenesulfonyl-α-D-galactopyranoside by super hydride simultaneously achieves deoxygenation at C-3 and C-6 to generate exclusively abequose. Both approaches suffer from the limitation that they offer no convenient synthetic strategy to differentiate the 2 and 4 hydroxyl groups of the resulting 3,6-dideoxyhexoses. In synthetic strategies to build complex antigen structures it is frequently necessary to introduce these monosaccharides in a form that permits selective manipulation at

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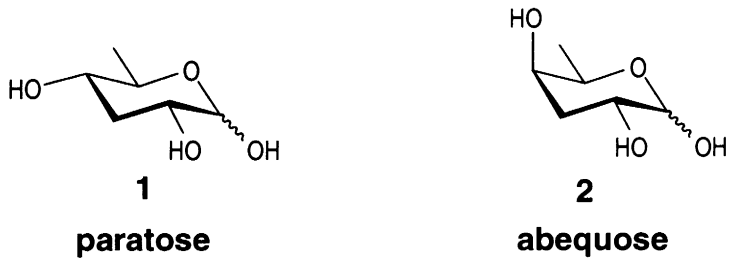


Fig. 1.

either OH-2 or OH-4. To date, methods to permit this have been limited. For example, one project to study enthalpy–entropy compensation required a tether between OH-2 of abequose and OH-2 of galactose of the trisaccharide αGal(1→2)[αAbe(1→3)]αMan(1→OMe), the epitope of *Salmonella* serotype B. This called for an abequose precursor that had different protecting groups at OH-2 and OH-4.[14] Attempts at direct regioselective monobenzylation on OH-2 or OH-4 of abequose proved to be inefficient.

In this paper, we report a facile and effective method based on 1,*2*-*O*-propylidene acetals of glucose and galactose for the synthesis of both phenyl 2-*O*-acetyl-4-*O*-benzyl-3,6-dideoxy-1-thio-D-*ribo*-hexopyranoside **3** and phenyl 2-*O*-acetyl-4-*O*-benzyl-3,6-dideoxy-1-thio-D-*xylo*-hexopyranoside **4**, in excellent overall yield (Fig. 2).

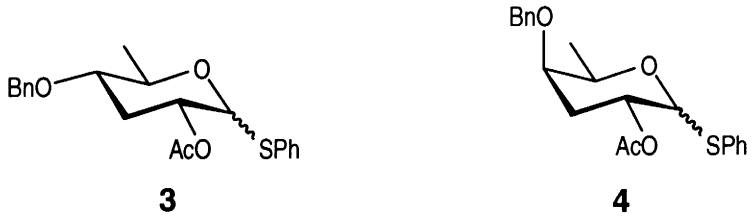


Fig. 2.

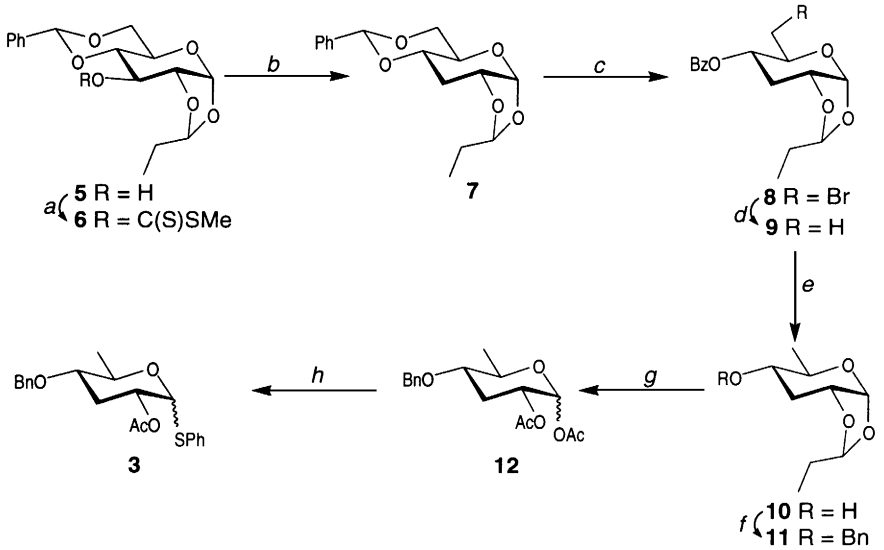
2. Results and discussion

Use of 1,2-*O*-propylidene acetals for protection of the 1,2 positions of glucose[15] and galactose[16] is a known but not widely adopted synthetic strategy. Allyl glycosides prepared by the Fischer glycosidation are converted to 4,6-*O*-benzylidene acetals and, after isomerisation of the allyl ether, the prop-1-enyl glycosides are readily transformed to the 1,2-acetal under acid catalysis.[15,16] Recently, Zagar and Scharf[17] successfully used this protecting group to prepare a 6-deoxyglucose unit in the synthesis of flambamycin, curamycin and avilamycin. The preparation of 3,6-dideoxy sugars using 1,2-*O*-propylidene acetal as the central protection strategy presents several advantages: (a) it is stable under various reaction conditions; (b) it can be easily removed to facilitate the conversion of the corresponding intermediates to glycosyl donors; and (c) the synthesis of the 1,2-*O*-propylidene derivatives can be performed on a large scale.[15]

*2.1. Synthesis of paratose derivative **3***

The synthesis of paratose (Scheme 1) started from 4,6-*O*-benzylidene-1,2-*O*-propylidene-α-D-glucopyranose **5**, prepared according to Collins et al.[15] Methyl xanthate **6** was prepared in virtually quantitative yield (97%) via a two-step procedure (NaH/CS_2/imidazole, MeI). Barton[18] radical

deoxygenation afforded the 3-deoxy compound **7** in excellent yield (95%). The benzylidene acetal of compound **7** underwent Hanessian–Hullar ring opening[19] to regioselectively introduce a bromide at the 6 position (→**8**) in 80% yield. The 1,2-*O*-propylidene protected paratose **9** was obtained in 95% yield after hydrogenation of the 6-bromo derivative **8** in the presence of potassium bicarbonate. The 4-benzoate was smoothly removed under Zemplen transesterification conditions (→**10**, 96% yield). When the hydrogenolysis of compound **8** was carried out on larger scale, simultaneous debenzoylation occurred, and compound **10** was obtained in 78% yield. After protecting the OH-4 group as a benzyl ether, the 1,2-*O*-propylidene group was successfully removed under acidic conditions. The resulting diol was not purified but directly acetylated to afford the diacetate **12** in 90% yield over two steps. Compound **12** was smoothly transformed to the target paratose thioglycoside **3** in 91% yield by reaction with phenylthiotrimethysilane in the presence of trimethylsilyl trifluoromethanesulfonate. This glycosyl donor with well differentiated protecting groups at OH-2 and OH-4 has been successfully employed in our laboratory for the synthesis of *Trichinella* related oligosaccharide epitopes.[20]

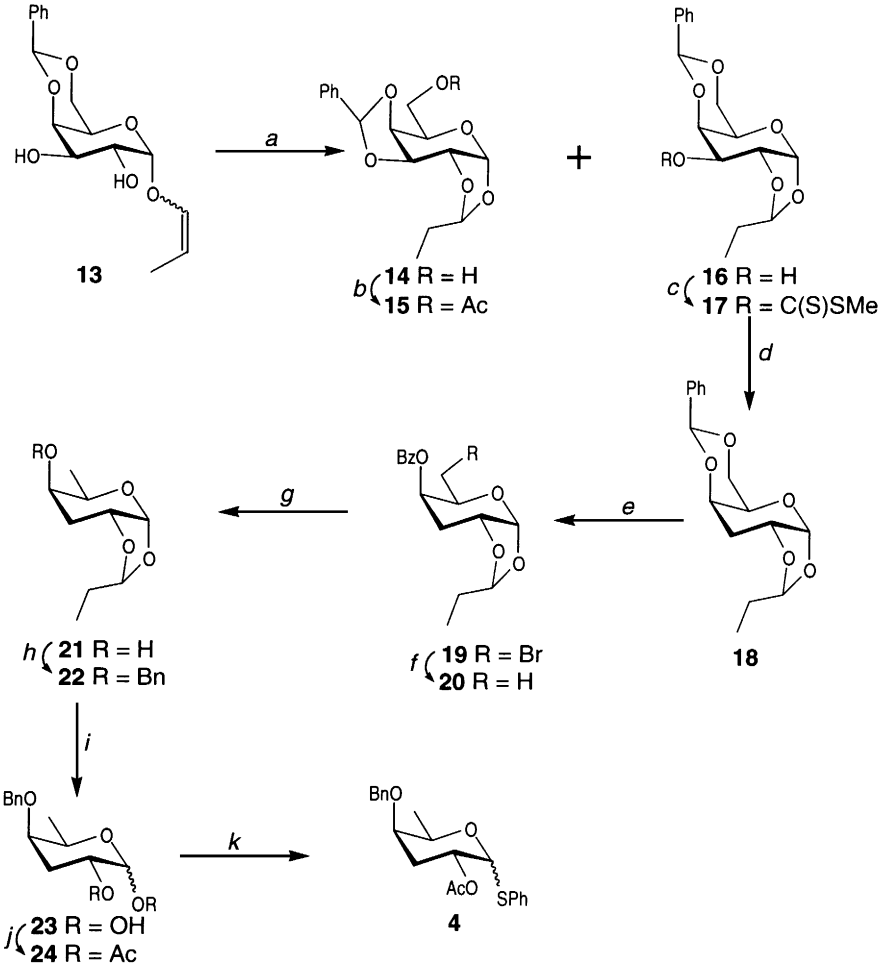


Scheme 1. (a) CS_2, NaH, imidazol, THF; then MeI; (b) Bu_3SnH, AIBN, toluene, reflux; (c) NBS, $BaCO_3$, CCl_4, reflux; (d) H_2/Pd–C, $NaHCO_3$, MeOH; (e) NaOMe, MeOH; (f) BnBr, NaH, DMF; (g) 10% H_2SO_4, THF, reflux; then Ac_2O, pyridine; (h) $PhSSiMe_3$, TMSOTf, toluene

*2.2. Synthesis of abequose derivative **4***

A similar synthetic route was applied for the preparation of abequose derivative **4** (Scheme 2). The synthesis of 1,2-*O*-propylidene compound **16** was reported by Gigg and Warren[16] in 57% yield by refluxing compound **13** in ethyl acetate in the presence of *p*-toluenesulfonic acid for 3 h. Initially, our attempts to reproduce this reaction were problematic. When compound **13** was treated with camphor sulfonic acid in refluxing ethyl acetate, a less polar side product was formed (TLC), in addition to the expected 1,2-isopropylidene acetal derivative **16**. The yield of this side product varied between batches. When the reaction mixture was subjected to prolonged treatment with acid, the side product predominated (up to 73% isolated yield). NMR showed that this compound is a single isomer bearing a benzylidene and propylidene acetals. The proton NMR of the acetylated product showed only two H-6 downfield shifted protons. The structure of this acetylated compound was assigned as 6-*O*-acetyl-3,4-*O*-benzylidene-1,2-*O*-

propylidene-α-D-galactopyranose **15**. The side product was therefore concluded to be the corresponding 6-OH (**14**). It is presumed that, during the acid catalysed reaction, the 4,6-*O*-benzylidene migrated to give the thermodynamically favoured dioxolane ring.

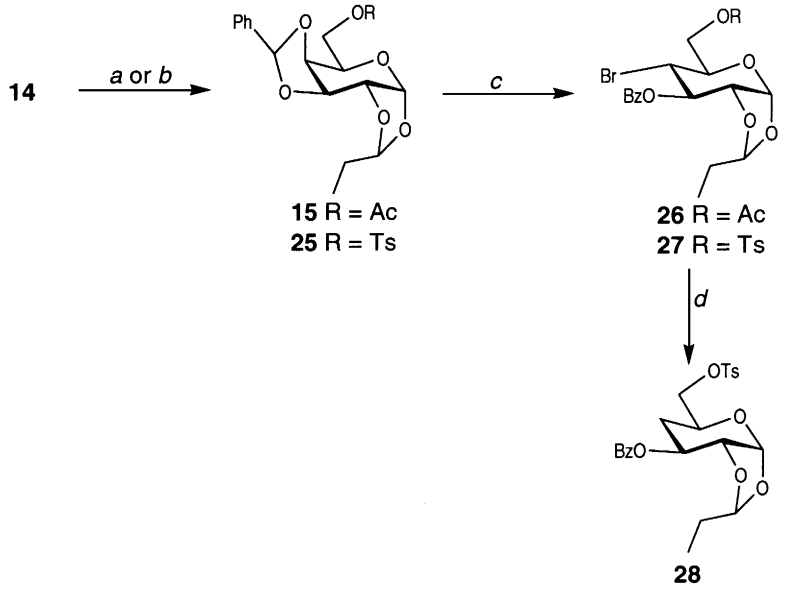


Scheme 2. (a) CSA, EtOAc, reflux or CSA, MS 4 Å, EtOAc, reflux; (b) Ac_2O, pyridine; (c) CS_2, NaH, imidazole, THF; then MeI; (d) Bu_3SnH, $NCC_6H_{10}N{=}NC_6H_{10}CN$, toluene, reflux; (e) NBS, $BaCO_3$, CCl_4, reflux; (f) H_2Pd–C, $NaHCO_3$, MeOH; (g) NaOMe, MeOH; (h) BnBr, NaH, DMF; (i) 10% H_2SO_4, THF, reflux; (j) Ac_2O, pyridine; (k) $BF_3{\cdot}OEt_2$, PhSH, CCl_4, MS 4 Å

The configuration at the benzylidene carbon atom was assigned as *endo* by a 2D T-ROESY experiment, as the benzylidene proton interacts only with ring protons, H-4 and H-3. Laboratory experience indicates that molecular sieves are slightly basic, so the 1,2-*O*-propylidene acetal formation was carried out in the presence of 4 Å molecular sieves. Under these conditions the yield of the 4,6-*O*-benzylidene isomer **16** was dramatically improved to 88% with only trace amounts of **14**. The molecular sieves by functioning as a base buffered the solution so that migration of the benzylidene acetal was minimised. A deoxygenation sequence similar to that used for compound **3** was applied. The xanthate **17** was first prepared from **16** in the same manner as described for **6** (→**17**, 93% yield). Barton radical deoxygenation gave the 3-deoxy compound **18** in almost quantitative yield. Deoxygenation at C-6 was realised by NBS mediated opening of the 4,6-benzylidene acetal (→**19**), followed by hydrogenation of the bromide **19** to give 3,6-dideoxy

derivative **20** in good to high yields (for both steps 77% and 98%). After exchanging the benzoate for a benzyl group at the 4 position (→**21**, 98%, →**22**, 95%), the desired target compound **4** was prepared following a three-step reaction sequence: acidic removal of the 1,2-*O*-propylidene acetal (→**23**, 91%), acetylation of the diol (→**24**, 96%), and conversion of the diacetate to thioabequoside **4** by treatment of **24** with thiophenol in the presence of $BF_3 \cdot OEt_2$ (93%).

The NBS mediated ring opening (Hanessian–Hullar reaction) of benzylidene acetals involving two secondary hydroxyl groups of carbohydrates (such as the case of rhamnose or galactose) has been reported in the literature[4,21,22] to give mainly the product in which bromide attacks the carbon bearing an equatorial oxygen. In our case, if this ring opening pattern holds, we could use the isomerised benzylidene acetal **14** to prepare compound **4** (Scheme 3). We initially tried this reaction with compound **15**, and surprisingly only the compound **26** in which bromide had attacked the carbon bearing an axial substituent was isolated in a yield of 79%. This is opposite to the expected regioselectivity and also to our previously reported observations during the synthesis of abequose[7] and colitose.[23] In order to force the bromide attack at the 3 position, we decided to introduce a group larger than acetate to the 6 position. A tosylate was the choice, because it can be easily reduced to the 6-deoxy derivative. Thus, the 6-hydroxyl group of **14** was quantitatively tosylated to give compound **25**. However, when this compound was subjected to the Hanessian–Hullar reaction, again, the 4-bromo-3-*O*-benzoyl derivative **27** was the exclusive product (86% yield). When the 4-bromo compound was subjected to hydogenolysis, the 4-deoxy compound **28** was obtained in 96% yield.



Scheme 3. (a) Ac_2O, pyridine, rt; (b) NaH, TsCl; (c) NBS, $BaCO_3$, CCl_4, reflux; (d) H_2/Pd–C, $NaHCO_3$, MeOH

Computer modelling reveals that compound **15** does not adopt a chair conformation, but an envelope conformation (^{O}E) with C-1, C-2, C-3, C-4 and C-5 aligned in one plane and the ring oxygen out of the plane. This is due to the extreme constraints introduced by the tricyclic system. The axial and equatorial differences of the chair form do not exist in this system anymore. However, from the model, it can be clearly observed that the C-3 position rather than the C-4 position experiences greater steric hindrance from the dioxolane ring at C-1 and C-2 and its ethyl side. This explains why the bromide prefers to attack at the C-4 but not at the C-3 position.

In summary, we have developed a facile and effective route for the synthesis of two 3,6-dideoxyhexoses. The route is well suited to the efficient synthesis of stable glycosyl donors that contain orthogonal protecting groups at OH-2 and OH-4. Glycosyl donors of this type have facilitated the preparation of structurally diverse oligosaccharide epitopes (Fig. 3).

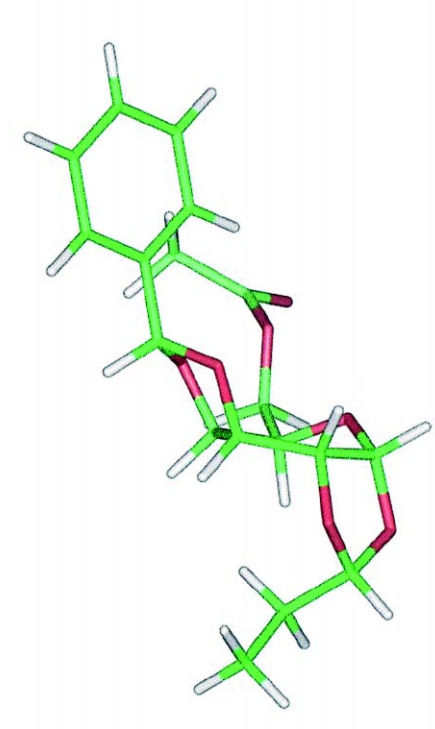


Fig. 3.

3. Experimental

Optical rotations were measured with a Perkin–Elmer 241 polarimeter at 22±2°C. Analytical TLC was performed on silica gel 60-F_{254} (E. Merck, Darmstadt) with detection by quenching of fluorescence and/or by charring with sulfuric acid. All commercial reagents were used as supplied and chromatography solvents were distilled prior to use. Column chromatography was performed on silica gel 60 (E. Merck 40–60 μm, Darmstadt). ^{1}H NMR spectra were recorded at 300 MHz (Varian) or 600 MHz (Varian). The first order proton chemical shifts δ_H are referenced to either internal $CDCl_3$ (δ_H 7.24, $CDCl_3$) or internal acetone (δ_H 2.225, D_2O). HMQC NMR spectra were recorded at 300 MHz (Varian) or 600 MHz (Varian). The ^{13}C chemical shifts δ_C are referenced to internal $CDCl_3$ (δ_C 77.00, $CDCl_3$). Organic solutions were dried prior to concentration under vacuum at <40°C (bath). Microanalyses and electrospray mass spectra were carried out by the analytical services of this department.

*3.1. 4,6-*O*-Benzylidene-3-*O*-(methylthio)thiocarbonyl-1,2-*O*-propylidene-α-*D*-glucopyranose* **6**

NaH (2.8 g, 110.9 mmol) was added by small portions to alcohol **5**[15] (14.0 g, 46.2 mmol) dissolved in anhydrous THF (220 mL), and imidazole (158 mg, 2.3 mmol) was added. After stirring at room

temperature for 1.5 h, CS_2 (14 mL, 231.0 mmol) was added and the mixture was stirred at room temperature for 3.5 h. MeI (14 mL, 225.0 mmol) was added and the reaction was continued for another 1.5 h. The mixture was ice-cooled and the reaction quenched with MeOH (5 mL). After concentration under reduced pressure, the residue was dissolved in EtOAc (500 mL), and successively washed with HCl (1N, 1×200 mL), $NaHCO_3$ (satd, 200 mL) and brine (1×200 mL). The organic phase was separated, dried over anhydrous Na_2SO_4 and evaporated to afford the crude material **6** (17.6 g, 97.3% yield). NMR indicated that this material was sufficiently pure to be used for the next step without further purification. A small analytically pure sample was obtained by chromatography on silica gel using 30% EtOAc–hexane. $[\alpha]_D^{22}$ +10.5 (*c* 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.45 (m, 2H, Ph), 7.32–7.36 (m, 3H, Ph), 6.17 (dd, 1H, *J* 2.6 Hz, 7.1 Hz, H-3), 5.55 (d, 1H, *J* 4.5 Hz, H-1), 5.54 (s, 1H, PhCH), 4.89 (t, 1H, *J* 4.8 Hz, CH_3CH_2CH), 4.40 (dd, 1H, *J* 5.1 Hz, 10.5 Hz, H-6a), 4.13 (dd, 1H, *J* 2.6 Hz, 4.9 Hz, H-2), 4.02 (d't', 1H, *J* 5.0 Hz, 9.9 Hz, H-5), 3.92 (dd, 1H, *J* 7.1 Hz, 9.9 Hz, H-4), 3.72 (t, 1H, *J* 9.9 Hz, H-6b), 2.59 (s, 3H, SMe), 1.82 (m, 2H, CH_3CH_2CH), 1.02 (t, 3H, J 7.5 Hz, CH_3CH_2CH). High res. ES-MS: calcd for $C_{18}H_{22}O_6S_2Na^+$: 421.07555; found: 421.07546. Anal. calcd for $C_{18}H_{22}O_6S_2$: C, 54.25; H, 5.56. Found: C, 54.03; H, 5.55.

*3.2. 4,6-*O*-Benzylidene-3-deoxy-1,2-*O*-propylidene-α-*D*-ribo-hexopyranose **7***

A solution containing AIBN (100 mg, 0.5 mmol) and tributyltin hydride (27 mL, 97.8 mmol) in anhydrous toluene (270 mL) was added dropwise over a 1.5 h period to compound **6** (31.7 g, 79.5 mmol) dissolved in anhydrous toluene (450 mL) heated at reflux. The reaction was continued for 16 h. The pure deoxygenated compound **7** (22.0 g, 94.6% yield) was obtained by column chromatography on silica gel (hexane→10% EtOAc–hexane). $[\alpha]_D^{22}$ +62.5 (*c* 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.48 (m, 2H, Ph), 7.32–7.39 (m, 3H, Ph), 5.52 (s, 1H, PhCH), 5.38 (d, 1H, *J* 4.8 Hz, H-1), 4.85 (t, 1H, *J* 4.8 Hz, CH_3CH_2CH), 4.34 (dd, 1H, *J* 5.0 Hz, 10.4 Hz, H-6a), 4.10 (d't', 1H, *J* 4.5 Hz, 7.2 Hz, H-2), 3.98 (d't', 1H, *J* 5.1 Hz, 10 Hz, H-5), 3.61–3.71 (m, 2H, H-4+H-6b), 2.47 (d't', 1H, *J* 7.3 Hz, 14.5 Hz, H-3a), 2.00 (ddd, 1H, *J* 4.2 Hz, 9.1 Hz, 14.4 Hz, H-3e), 1.79 (dq, 2H, J 4.8 Hz, 7.6 Hz, CH_3CH_2CH), 1.02 (t, 3H, J 7.5 Hz, CH_3CH_2CH). High res. ES-MS: calcd for $C_{16}H_{20}O_5Na^+$: 315.12084; found: 315.12080. Anal. calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.31; H, 6.89.

*3.3. 4-*O*-Benzoyl-6-bromo-3,6-dideoxy-1,2-*O*-propylidene-α-*D*-ribo-hexopyranose **8***

Compound **7** (18.0 g, 61.6 mmol) was dissolved in anhydrous CCl_4 (450 mL), *N*-bromosuccinimide (16.0 g, 89.9 mmol) and $BaCO_3$ (24.3 g, 123.1 mmol) were added, and the mixture was refluxed for 2 h. The mixture was filtered and the organic solution was concentrated under reduced pressure. After chromatography on silica gel (20% EtOAc–hexane), the bromide **8** (18.4 g, yield 80%) was obtained as a white foam. $[\alpha]_D^{22}$ +29.3 (*c* 0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.02 (m, 2H, Bz), 7.56 (m, 1H, Bz), 7.43 (m, 2H, Bz), 5.52 (d, 1H, *J* 5.3 Hz, H-1), 5.27 ('t', *J* 7.6 Hz, 1H, H-4), 4.85 (t, 1H, *J* 4.9 Hz, CH_3CH_2CH), 4.24 (ddd, 1H, *J* 3.3 Hz, 5.4 Hz, 7.9 Hz, H-5), 4.14 (d't', 1H, *J* 2.9 Hz, 5.3 Hz, H-2), 3.62 (dd, 1H, *J* 3.3 Hz, 11.1 Hz, H-6a), 3.53 (dd, 1H, *J* 5.3 Hz, 11.1 Hz, H-6b), 2.34 (ddd, 1H, *J* 0.9 Hz, 2.9 Hz, 16.3 Hz, H-3e), 2.17 (ddd, 1H, *J* 2.9 Hz, 7.2 Hz, 16.3 Hz, H-3a), 1.87 (m, 2H, CH_3CH_2CH), 1.06 (t, 3H, *J* 7.6 Hz, CH_3CH_2CH). High res. ES-MS: calcd for $C_{16}H_{19}O_5BrNa^+$: 393.03135; found: 393.03157. Anal. calcd for $C_{16}H_{19}O_5Br$: C, 51.77; H, 5.16. Found: C, 48.71; H, 4.66.

3.4. 4-O-Benzoyl-3,6-dideoxy-1,2-O-propylidene-α-D-ribo-hexopyranose **9**

A mixture of bromide **8** (428 mg, 1.15 mmol), $KHCO_3$ (115 mg, 1.27 mmol) and 10% Pd–C (100 mg) in MeOH (50 mL) was hydrogenated for 18 h at room temperature. The catalyst was filtered off and the filtrate was concentrated. Compound **9** (320 mg, 95% yield) was obtained by chromatography on silica gel (20% EtOAc–hexane). When this reaction was carried out on a large scale, partial debenzoylation occurred. Addition of more $KHCO_3$ (1.3 equiv.) allowed the formation of completely debenzoylated product (see below). $[\alpha]_D^{22}$ +40.2 (*c* 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.03 (m, 2H, Bz), 7.56 (m, 1H, Bz), 7.42 (m, 2H, Bz), 5.42 (d, 1H, *J* 5.2 Hz, H-1), 4.96 (ddd, 1H, *J* 1.7 Hz, 5.8 Hz, 7.6 Hz, H-4), 4.83 (t, 1H, *J* 4.9 Hz, CH_3CH_2CH), 4.13 (dq, 1H, *J* 1.8 Hz, 6.3 Hz, H-5), 4.08 (d't', 1H, *J* 3.0 Hz, 5.2 Hz, H-2), 2.25 (d't', 1H, *J* 2.3 Hz, 16.5 Hz, H-3e), 2.17 (ddd, 1H, *J* 3.2 Hz, 7.2 Hz, 16.5 Hz, H-3a), 1.87 (dq, 2H, *J* 5.1 Hz, 7.6 Hz, CH_3CH_2CH), 1.28 (d, 3H, *J* 6.3 Hz, H-6), 1.07 (t, 3H, *J* 7.6 Hz, CH_3CH_2CH). High res. ES-MS: calcd for $C_{16}H_{20}O_5Na^+$: 315.12084; found: 315.12079. Anal. calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.52; H, 6.91.

3.5. 3,6-Dideoxy-1,2-O-propylidene-α-D-ribo-hexopyranose **10**

Method A: Compound **9** (260 mg, 0.89 mmol) was dissolved in anhydrous MeOH (10 mL), a catalytic amount of MeONa was added, and the reaction was continued for 3 h at room temperature. The mixture was neutralised with Dowex 50W (H^+) resin; the residue was purified by chromatography on silica gel using 30% EtOAc–hexane as eluent to afford **10** (161 mg, 96%).

Method B: A mixture of bromide **8** (18.4 g, 49.6 mmol), $KHCO_3$ (6.5 g, 64.8 mmol) and 10% Pd–C (2.8 g) in MeOH (750 mL) was hydrogenated for 48 h at room temperature. The catalyst was filtered off and the solution was concentrated. Compound **10** (7.25 g, 78% yield) was obtained by chromatography on silica gel (30% EtOAc–hexane). $[\alpha]_D^{22}$ −35.2 (*c* 1.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.39 (d, 1H, *J* 5.1 Hz, H-1), 4.77 (t, 1H, *J* 5.1 Hz, CH_3CH_2CH), 4.10 (d't', 1H, *J* 3.2 Hz, 5.2 Hz, H-2), 3.75 (dq, 1H, *J* 6.5 Hz, 6.5 Hz, H-5), 3.50 (d't', 1H, *J* 1.0 Hz, 6.3 Hz, H-4), 2.18 (ddd, 1H, *J* 1.0 Hz, 3.4 Hz, 15.7 Hz, H-3a), 1.94 (ddd, 1H, *J* 2.4 Hz, 6.3 Hz, 15.7 Hz, H-3b), 1.79 (m, 2H, CH_3CH_2CH), 1.28 (d, 3H, *J* 6.5 Hz, H-6), 1.07 (t, 3H, *J* 7.6 Hz, CH_3CH_2CH). High res. ES-MS: calcd for $C_9H_{16}O_4Na^+$: 211.09463; found: 211.09500. Anal. calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.23; H, 8.36.

3.6. 4-O-Benzyl-3,6-dideoxy-1,2-O-propylidene-α-D-ribo-hexopyranose **11**

To a solution of alcohol **10** (3.3 g, 17.7 mmol) in anhydrous DMF (50 mL), NaH (95%, 1.3 g, 53.0 mmol) was added. After 5 min, benzyl bromide (5.3 mL, 44.2 mmol) was added dropwise. The reaction was continued for 2 h at room temperature and MeOH (2 mL) was added to quench the reaction. The mixture was diluted with EtOAc (150 mL), washed with 5% brine (2×75 mL), dried over Na_2SO_4 and concentrated. The pure compound **11** (4.4 g, 90% yield) was obtained by chromatography on silica gel (10% EtOAc–hexane). $[\alpha]_D^{22}$ +74.8 (*c* 0.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.23–7.36 (m, 5H, Bn), 5.33 (d, 1H, *J* 5.2 Hz, H-1), 4.78 (t, 1H, *J* 5.0 Hz, CH_3CH_2CH), 4.64 (d, 1H, *J* 12.0 Hz, Bn), 4.43 (d, 1H, *J* 12.0 Hz, Bn), 4.05 ('t', 1H, *J* 3.3 Hz, 5.1 Hz, H-2), 3.92 (dq, 1H, *J* 6.3 Hz, 8.4 Hz, H-5), 3.33 (d't', 1H, *J* 2.0 Hz, 8.1 Hz, H-4), 2.24 (d't', 1H, *J* 2.5 Hz, 15.7 Hz, H-3e), 1.91 (ddd, 1H, *J* 3.8 Hz, 7.7 Hz, 15.7 Hz, H-3b), 1.81 (m, 2H, CH_3CH_2CH), 1.22 (d, 3H, *J* 6.3 Hz, H-6), 1.02 (t, 3H, *J* 7.6 Hz, CH_3CH_2CH). High res. ES-MS: calcd for $C_{16}H_{22}O_4Na^+$: 301.14158; found: 301.14199. Anal. calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.34; H, 7.77.

3.7. 1,2-Di-O-acetyl-4-O-benzyl-3,6-dideoxy-α,β-D-ribo-hexopyranose **12**

To a solution of compound **11** (3.9 g, 14.0 mmol) in THF (237 mL) was added a 10% aqueous solution of H_2SO_4 (59 mL) and the reaction was heated to 65°C for 3 h. The mixture was diluted with CH_2Cl_2 (500 mL), washed with saturated $NaHCO_3$ (1×200 mL), brine (1×200 mL), dried over Na_2SO_4 and concentrated. The residue was acetylated with a mixture of pyridine (50 mL) and acetic anhydride (50 mL) overnight at room temperature. The reaction was concentrated under reduced pressure and the diacetate **12** (4.1 g, 90% yield) was obtained as an anomeric mixture (α:β, 40:60) by chromatography on silica gel (20% EtOAc–hexane). ^{1}H NMR (300 MHz, $CDCl_3$): α-isomer: δ 7.25–7.35 (m, 5H, Bn), 6.11 (d, 1H, *J* 3.3 Hz, H-1), 4.89 (ddd, 1H, *J* 3.5 Hz, 4.8 Hz, 12.5 Hz, H-2), 4.62 (d, 1H, *J* 11.4 Hz, Bn), 4.46 (d, 1H, *J* 11.4 Hz, Bn), 3.78 (dq, 1H, *J* 6.2 Hz, 9.3 Hz, H-5), 3.20 (m, 1H, H-4), 2.36 (d't', 1H, *J* 4.8 Hz, 11.5 Hz, H-3e), 2.10 (s, 3H, Ac), 2.00 (s, 3H, Ac), 1.85 (d't', 1H, *J* 11.3 Hz, 11.3 Hz, H-3a), 1.24 (d, 3H, *J* 6.2 Hz, H-6). β-isomer: δ 7.25–7.35 (m, 5H, Bn), 5.64 (d, 1H, *J* 8.2 Hz, H-1), 4.76 (ddd, 1H, *J* 5.3 Hz, 8.2 Hz, 11.7 Hz, H-2), 4.59 (d, 1H, *J* 11.5 Hz, Bn), 4.43 (d, 1H, *J* 11.4 Hz, Bn), 3.58 (dq, 1H, *J* 6.0 Hz, 9.0 Hz, H-5), 3.20 (m, 1H, H-4), 2.65 (d't', 1H, *J* 4.8 Hz, 12.1 Hz, H-3e), 2.07 (s, 3H, Ac), 2.02 (s, 3H, Ac), 1.53 (d't', 1H, *J* 11.3 Hz, 11.3 Hz, H-3b), 1.28 (d, 3H, *J* 6.0 Hz, H-6). High res. ES-MS: calcd for $C_{17}H_{22}O_6Na^+$: 345.13141; found: 345.13155. Anal. calcd for $C_{17}H_{22}O_6$: C, 63.33; H, 6.88. Found: C, 63.28; H, 6.97.

3.8. Phenyl 2-O-acetyl-4-O-benzyl-3,6-dideoxy-1-thio-α,β-D-ribo-hexopyranoside **3**

To an ice-cooled mixture of the diacetate **12** (2.47 g, 7.66 mmol) and 4 Å molecular sieves (4.0 g) in anhydrous toluene (60 mL) were added phenylthiotrimethylsilane (3.73 mL, 19.15 mmol) and TMSOTf (600 μl, 3.3 μmol). The mixture was stirred at room temperature for 6 h. Et_3N (5 mL) was added to quench the reaction. The molecular sieves were filtered off and the filtrate was concentrated. The mixture was purified by column chromatography on silica gel (5%→10% EtOAc–hexane) to afford the thioglycosides **3** as an inseparable α/β mixture(α:β, 37:73, 3.63 g, 91% yield). ^{1}H NMR ($CDCl_3$): α-isomer: δ 7.22–7.48 (m, 10H, Ar), 5.66 (d, 1H, *J* 5.1 Hz, H-1), 5.00 (d't', 1H, *J* 4.8 Hz, 12.5 Hz, H-2), 4.64 (d, 1H, *J* 11.5 Hz, Bn), 4.49 (d, 1H, *J* 11.4 Hz, Bn), 4.19 (dq, 1H, *J* 6.2 Hz, 9.2 Hz, H-5), 3.22 (ddd, 1H, *J* 4.4 Hz, 9.3 Hz, 11.0 Hz, H-4), 2.37 (d't', 1H, *J* 4.6 Hz, 11.9 Hz, H-3e), 2.08 (s, 3H, Ac), 1.86 (d't', 1H, *J* 12.1 Hz, 12.1 Hz, H-3a), 1.25 (d, 3H, *J* 6.2 Hz, H-6). β-isomer: δ 7.22–7.48 (m, 10H, Ar), 4.72 (ddd, 1H, *J* 4.9 Hz, 9.9 Hz, 11.0 Hz, H-2), 4.64 (d, 1H, *J* 9.9 Hz, H-1), 4.59 (d, 1H, *J* 11.5 Hz, Bn), 4.35 (d, 1H, *J* 11.4 Hz, Bn), 3.44 (dq, 1H, *J* 6.2 Hz, 9.0 Hz, H-5), 3.19 (ddd, 1H, *J* 4.4 Hz, 9.2 Hz, 11.0 Hz, H-4), 2.37 (d't', 1H, *J* 4.8 Hz, 11.9 Hz, H-3e), 2.08 (s, 3H, Ac), 1.53 (d't', 1H, *J* 11.7 Hz, 11.7 Hz, H-3b), 1.34 (d, 3H, *J* 6.0 Hz, H-6). High res. ES-MS: calcd for $C_{21}H_{24}O_4SNa^+$: 395.12930; found: 395.12996. Anal. calcd for $C_{21}H_{24}O_4S$: C, 67.72; H, 6.49. Found: C, 67.78; H, 6.65.

3.9. 4,6-O-Benzylidene-1,2-O-propylidene-α-D-galactopyranose **16** and 3,4-O-benzylidene-(R)-1,2-O-propylidene-α-D-galactopyranose **14**

Method A: Prop-1′-enyl 4,6-*O*-benzylidene-α-D-galactopyranoside[16] **13** (30 g, 96 mmol) and camphor sulfonic acid (1.5 g) were dissolved in freshly distilled ethyl acetate (500 mL); the mixture was refluxed at 90°C under argon for 5 h. The reaction was quenched with Et_3N (5 mL). The solution was washed with water (1×150 mL), dried over Na_2SO_4 and concentrated. Chromatography of the resulting residue on silica gel with hexane:EtOAc (3:2) gave the 3,4-*O*-benzylidene isomer **14** (22.0 g, 73% yield) and 4,6-*O*-benzylidene isomer **16** (4.5 g, 15% yield).

Method B: A solution of prop-1′-enyl 4,6-*O*-benzylidene-α-D-galactopyranoside **13** (1.5 g, 4.8 mmol), camphor sulfonic acid (130 mg) and 4 Å molecular sieves (1.0 g) in freshly distilled ethyl acetate (80 mL) was heated to 90°C under argon for 72 h. The mixture was then neutralised with triethylamine (2 mL). The molecular sieves were filtered off, and the organic phase was washed with water (1×40 mL), dried over Na_2SO_4 and concentrated. Chromatography of the resulting residue on silica gel with hexane:EtOAc (3:2) gave **16** (1.32 g, 88%).

Compound **16** has: $[\alpha]_D^{22}$ +36.8 (*c* 0.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.34–7.50 (m, 5H, Ph), 5.73 (d, 1H, *J* 4.0 Hz, H-1), 5.58 (s, 1H, PhCH), 4.95 (t, 1H, *J* 4.8 Hz, CH_3CH_2CH), 4.36 (dd, 1H, *J* 1.0 Hz, 12.7 Hz, H-6a), 4.28 (dd, 1H, *J* 2.2 Hz, 4.3 Hz, H-4), 4.1 (dd, 1H, *J* 2.3 Hz, 12.8 Hz, H-6b), 3.99–4.03 (m, 2H, H-2+H-3), 3.86 (m, 1H, H-5), 2.68 (bs, 1H, 3-OH), 1.75 (dq, 2H, *J* 5.0 Hz, 7.5 Hz, CH_3CH_2CH), 1.00 (t, 3H, *J* 7.5 Hz, CH_3CH_2CH). ^{13}C NMR ($CDCl_3$, from HMQC): δ 126.2–129.2 (m, Ph), 104.0 (CH_3CH_2CH), 100.6 (PhCH), 97.8 ($J_{C1,H1}$ 177.6 Hz, C-1), 76.1 (C-2), 72.0 (C-4), 69.8 (C-6), 69.2 (C-3), 63.6 (C-5), 27.3 (CH_3CH_2CH), 7.2 (CH_3CH_2CH). High res. ES-MS: calcd for $C_{16}H_{20}O_6Na^+$: 331.11576; found: 331.11529. Anal. calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.51; H, 6.77. The structure of this compound was also confirmed by acetylation of the 3-hydroxy group. The *3*-*O*-acetyl-4,6-*O*-benzylidene-1,2-*O*-propylidene-α-D-galactopyranose has: $[\alpha]_D^{22}$ +70.0 (*c* 0.3, MeOH). ^{1}H NMR ($CDCl_3$): δ 7.34–7.47 (m, 5H, Ph), 5.84 (d, 1H, *J* 4.4 Hz, H-1), 5.47 (s, 1H, PhCH), 5.02 (t, 1H, *J* 4.9 Hz, CH_3CH_2CH), 4.99 (dd, 1H, *J* 2.8 Hz, 6.8 Hz, H-3), 4.40 (dd, 1H, *J* 2.2 Hz, 2.8 Hz, H-4), 4.36 (dd, 1H, *J* 1.5 Hz, 12.6 Hz, H-6a), 4.20 (dd, 1H, *J* 4.4 Hz, 6.8 Hz, H-2), 4.05 (dd, 1H, *J* 1.8 Hz, 12.6 Hz, H-6b), 3.91 (m, 1H, H-5), 2.13 (s, 3H, OAc), 1.75 (dq, 2H, *J* 5.6 Hz, 7.7 Hz, CH_3CH_2CH), 0.98 (t, 3H, *J* 7.5 Hz, CH_3CH_2CH). High res. ES-MS: calcd for $C_{18}H_{22}O_7Na^+$: 373.12632; found: 373.12643. Anal. calcd for $C_{18}H_{22}O_7$: C, 61.71; H, 6.33. Found: C, 61.51; H, 6.47.

Compound **14** has: $[\alpha]_D^{22}$ −47.3 (*c* 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.26–7.66 (m, 5H, Ph), 5.74 (s, 1H, PhCH), 5.63 (d, 1H, *J* 5.1 Hz, H-1), 4.83 (t, 1H, *J* 4.9 Hz, CH_3CH_2CH), 4.70 (dd, 1H, *J* 2.4 Hz, 8.2 Hz, H-3), 4.33 (dd, 1H, *J* 1.8 Hz, 8.3 Hz, H-4), 4.22 (dd, 1H, *J* 2.4 Hz, 5.2 Hz, H-2), 4.02 (m, 1H, H-5), 3.90 (dd, 1H, *J* 7.2 Hz, 11.5 Hz, H-6a), 3.78 (dd, 1H, *J* 4.7 Hz, 11.6 Hz, H-6b), 1.97 (bs, 1H, 6-OH), 1.79 (m, 2H, CH_3CH_2CH), 1.30 (t, 3H, *J* 7.1 Hz, CH_3CH_2CH). ^{13}C NMR ($CDCl_3$, from HMQC): δ 126.2–130.0 (Ph), 104.2 (CH_3CH_2CH), 103.7 (PhCH), 95.7 ($J_{C1,H1}$ 181.7 Hz, C-1), 71.6, 71.5, 71.2 (C-2, 3, 4), 67.6 (C-5), 61.8 (C-6), 26.0 (CH_3CH_2CH), 7.6 (CH_3CH_2CH). Anal. calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.21; H, 6.75. Compound **14** was quantitatively acetylated using conventional methods and the corresponding 6-*O*-acetyl-3,4-*O*-(*R*)-benzylidene-1,2-*O*-propylidene-α-D-galactopyranose **15** has: $[\alpha]_D^{22}$ +9.6 (*c* 0.7, MeOH). ^{1}H NMR ($CDCl_3$): δ 7.51 (m, 2H, Ph), 7.34–7.40 (m, 3H, Ph), 5.75 (s, 1H, PhCH), 5.61 (d, 1H, *J* 5.1 Hz, H-1), 4.83 (t, 1H, *J* 4.9 Hz, CH_3CH_2CH), 4.69 (dd, 1H, *J* 2.5 Hz, 8.2 Hz, H-3), 4.36 (dd, 1H, *J* 4.7 Hz, 11.3 Hz, H-6a), 4.31 (dd, 1H, *J* 1.5 Hz, 8.1 Hz, H-4), 4.19–4.26 (m, 2H, H-2+H-6b), 4.16 (m, 1H, H-5), 2.06 (s, 3H, OAc), 1.77 (m, 2H, CH_3CH_2CH), 1.00 (t, 3H, *J* 7.5 Hz, CH_3CH_2CH). ^{13}C NMR ($CDCl_3$): δ 170.9 (CO), 136.0, 130.1, 128.5, 127.4 (Ph), 104.7 (CH_3CH_2CH), 103.1 (PhCH), 96.0 (C-1), 71.8, 71.6, 71.4 (C-2, 3, 4), 65.9 (C-5), 63.4 (C-6), 26.6 (CH_3CH_2CH), 20.9 (Ac), 8.2 (CH_3CH_2CH). High res. ES-MS: calcd for $C_{18}H_{22}O_7Na^+$: 373.12632; found: 373.12599. Anal. calcd for $C_{18}H_{22}O_7$: C, 61.71; H, 6.33. Found: C, 61.45; H, 6.24.

*3.10. 4,6-*O*-Benzylidene-3-*O*-(methylthio)thiocarbonyl-1,2-*O*-propylidene-α-D-galactopyranose **17***

Compound **16** (4.5 g, 14.6 mmol) was reacted with CS_2 and methylated with MeI using the method described for **6** (5.1 g, 89%). $[\alpha]_D^{22}$ +162.5 (*c* 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.16–7.66 (m, 5H, Ph), 5.87 (d, 1H, *J* 4.4 Hz, H-1), 5.84 (dd, 1H, *J* 2.9 Hz, 6.8 Hz, H-3), 5.48 (s, 1H, PhCH), 5.03 (t, 1H, *J* 4.9 Hz, CH_3CH_2CH), 4.65 (dd, 1H, *J* 2.1 Hz, 2.7 Hz, H-4), 4.39 (dd, 1H, *J* 4.4 Hz, 6.8 Hz, H-2), 4.37

(dd, 1H, *J* 1.8 Hz, 12.4 Hz, H-6a), 4.06 (dd, 1H, *J* 1.9 Hz, 12.6 Hz, H-6b), 3.95 (m, 1H, H-5), 2.57 (s, 3H, SCH_3), 1.76 (dq, 2H, *J* 4.5 Hz, 7.5 Hz, CH_3CH_2CH), 0.98 (t, 3H, *J* 7.6 Hz, CH_3CH_2CH). ^{13}C NMR ($CDCl_3$, from HMQC): δ 125.9–128.6 (Ph), 104.2 (CH_3CH_2CH), 101.0 (PhCH), 98.6 ($J_{C1,H1}$ 177.9 Hz, C-1), 81.8 (C-3), 73.3 (C-2), 72.1 (C-4), 70.1 (C-6), 65.0 (C-5), 27.6 (CH_3CH_2CH), 18.6 (SCH_3), 8.0 (CH_3CH_2CH). High res. ES-MS: calcd for $C_{18}H_{22}O_6S_2Na^+$: 421.07555; found: 521.07638. Anal. calcd for $C_{18}H_{22}O_6S_2$: C, 54.25: H, 5.56; S, 16.09. Found: C, 54.01; H, 5.66; S, 16.16.

3.11. 4,6-O-Benzylidene-3-deoxy-1,2-O-propylidene-α-D-xylo-hexopyranose ***18***

To a refluxing solution of **17** (900 mg, 2.3 mmol) in dry toluene (50 mL) was added a solution containing tributyltin hydride (1.31 g, 4.5 mmol) and azobis(cyclohexanecarbonitrile) (11.3 mg, 67.5 μmol) in dry toluene (30 mL) under argon. After 5 h, the mixture was concentrated. Chromatography of the resulting residue on silica gel with hexane:EtOAc (17:3) gave compound **18** (670 mg, 98%). $[\alpha]_D^{22}$ −30.5 (*c* 0.6, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.30–7.50 (m, 5H, Ph), 5.58 (d, 1H, *J* 5.1 Hz, H-1), 5.50 (s, PhCH), 4.76 (t, 1H, *J* 5.0 Hz, CH_3CH_2CH), 4.32 (dd, 1H, *J* 1.3 Hz, 12.9 Hz, H-6a), 4.26 (m, 1H, H-4), 4.15 (dd, 1H, *J* 2.8 Hz, 12.9 Hz, H-6b), 4.02 (m, 1H, H-2), 3.79 (m, 1H, H-5), 2.66 (ddd, 1H, *J* 2.9 Hz, 8.7 Hz, 15.7 Hz, H-3e), 1.92 (d't', *J* 4.4 Hz, 15.8 Hz, H-3a), 1.75 (m, 2H, CH_3CH_2CH). 1.01 (t, 3H, *J* 7.5 Hz, CH_3CH_2CH). ^{13}C NMR ($CDCl_3$, from HMQC): δ 125.8–128.0 (Ph), 104.0 (CH_3CH_2CH), 100.0 (PhCH), 97.2 (C-1), 71.4 (C-2), 69.7, 69.5 (C-4, 6), 61.7 (C-5), 28.1 (C-3), 26.3 (CH_3CH_2CH), 8.5 (CH_3CH_2CH). High res. ES-MS: calcd for $C_{16}H_{20}O_5Na^+$: 315.12084; found: 315.12072. Anal. calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.35; H, 7.02.

3.12. 4-O-Benzoyl-6-bromo-3,6-dideoxy-1,2-O-propylidene-α-D-xylo-hexopyranose ***19***

To a solution of **18** (600 mg, 2.05 mmol) in dry CCl_4 (20 mL), NBS (561 mg, 3.15 mmol) and barium carbonate (848 mg, 6.9 mmol) were added; the reaction was heated at 90°C for 30 min. The mixture was then cooled to room temperature and filtered through a thin pad of Celite. After concentration, chromatography of the resulting residue on silica gel with hexane:EtOAc (4: 1) afforded compound **19** (590 mg, 77%). $[\alpha]_D^{22}$ −58.6 (*c*1.2, MeOH). ^1H NMR ($CDCl_3$): δ 8.02 (m, 2H, Bz), 7.56 (m, 1H, Bz), 7.44 (m, 2H, Bz), 5.52 (d, 1H, *J* 5.2 Hz, H-1), 5.39 (ddd, 1H, *J* 4.1 Hz, 6.5 Hz, 8.4 Hz, H-4), 4.80 (t, 1H, *J* 5.0 Hz, CH_3CH_2CH), 4.38 (d't', 1H, *J* 4.0 Hz, 6.9 Hz, H-2), 4.07 (m, 1H, H-5), 3.52 (dd, 1H, *J* 6.6 Hz, 10.4 Hz, H-6a), 3.46 (dd, 1H, *J* 7.1 Hz, 10.4 Hz, H-6b), 2.91 (ddd, 1H, *J* 3.0 Hz, 8.4 Hz, 15.1 Hz, H-3e), 1.83–1.70 (m, 3H, H-3a+CH_3CH_2CH), 1.03 (t, 3H, *J* 7.5 Hz, CH_3CH_2CH). ^{13}C NMR ($CDCl_3$, from HMQC): δ 128.6–135.5 (Bz), 104.6 (CH_3CH_2CH), 97.6 (C-1), 72.0 (C-5), 67.9 (C-2), 66.1 (C-4), 28.2 (C-6), 28.0 (C-3), 21.8 (CH_3CH_2CH), 8.0 (CH_3CH_2CH). ES-MS: calcd for $C_{16}H_{19}O_5BrNa^+$: 393; found: 393. Anal. calcd for $C_{16}H_{19}BrO_5$: C, 51.70; H, 5.16. Found: C, 51.70; H, 4.81.

3.13. 4-O-Benzoyl-3,6-dideoxy-1,2-O-propylidene-α-D-xylo-hexopyranose ***20***

A solution of bromide **19** (4.95 g, 13.5 mmol), $KHCO_3$ (1.5 g, 15.0 mmol) and Pd–C (10%, 1.0 g) was hydrogenated for 3 days. The catalyst was removed by filtration and washed with MeOH and the filtrate was concentrated. Chromatography of the residue on silica gel with hexane:EtOAc (4:1) gave **20** (3.82 g, 98%). $[\alpha]_D^{22}$ −37.7 (*c* 0.5, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.05 (m, 2H, Bz), 7.56 (m, 1H, Bz), 7.44 (m, 2H, Bz), 5.46 (d, 1H, *J* 5.3 Hz, H-1), 5.26 (ddd, 1H, *J* 4.2 Hz, 7.0 Hz, 8.4 Hz, H-4), 4.8 (t, 1H, *J* 5.0 Hz, CH_3CH_2CH), 4.31 (dq, 1H, *J* 4.2 Hz, 6.6 Hz, H-5), 4.1 (d't', 1H, *J* 3.2 Hz, 5.41 Hz, H-2), 2.79 (ddd, 1H, *J* 3.2 Hz, 8.4 Hz, 15.1 Hz, H-3e), 1.79 (m, 3H, H-3a+CH_3CH_2CH), 1.23 (d, 3H, *J* 6.6 Hz,

H-6), 1.03 (t, 3H, *J* 7.5 Hz, C*H*$_3$CH$_2$CH). ^{13}C NMR ($CDCl_3$, from HMQC): δ 128.2–133.1 (Bz), 104.2 (CH$_3$CH$_2$*C*H), 97.0 (C-1), 72.4 (C-2), 68.5 (C-4), 64.2 (C-5), 28.0 (C-3), 26.4 (CH$_3$*C*H$_2$CH), 15.0 (C-6), 8.0 (*C*H$_3$CH$_2$CH). High res. ES-MS: calcd for $C_{16}H_{20}O_5Na^+$: 315.12084; found: 315.12114. Anal. calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.42; H, 6.97.

*3.14. 3,6-Dideoxy-1,2-*O*-propylidene-α-*D*-xylo-hexopyranose **21***

Compound **20** (3.26 g, 11.2 mmol) was debenzoylated similarly as described for **11** to yield compound **21** (2.0 g, 95%). $[\alpha]_D^{22}$ −46.1 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.37 (d, 1H, *J* 5.2 Hz, H-1), 4.75 (t, 1H, *J* 5.04 Hz, CH$_3$CH$_2$C*H*), 4.10 (dq, 1H, *J* 3.5 Hz, 6.2 Hz, H-5), 3.99 (d't', 1H, *J* 3.3 Hz, 5.3 Hz, H-2), 3.83 (ddd, 1H, *J* 3.5 Hz, 6.1 Hz, 8.0 Hz, H-4), 2.60 (ddd, 1H, *J* 3.1 Hz, 8.0 Hz, 15.3 Hz, H-3e), 1.74 (m, 2H, CH$_3$C*H*$_2$CH), 1.66 (ddd, 1H, *J* 3.9 Hz, 6.1 Hz, 15.4 Hz, H-3a), 1.21 (d, 3H, *J* 6.7 Hz, H-6), 0.99 (t, 3H, *J* 7.5 Hz, C*H*$_3$CH$_2$CH). ^{13}C NMR ($CDCl_3$, from HMQC): δ 103.5 (CH$_3$CH$_2$*C*H), 96.8 (C-1), 72.0 (C-2), 66.5 (C-5), 66.0 (C-4), 31.0 (C-3), 26.5 (CH$_3$*C*H$_2$CH), 14.6 (C-6), 7.8 (*C*H$_3$CH$_2$CH). High res. ES-MS: calcd for $C_{16}H_{16}O_4Na^+$: 211.09427; found: 211.09427. Anal. calcd for $C_{16}H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.55; H, 8.62.

*3.15. 4-*O*-Benzyl-3,6-dideoxy-1,2-*O*-propylidene-α-*D*-hexopyranose **22***

A solution of compound **21** (1.5 g, 8.0 mmol) in dry DMF (50 mL) was cooled to 4°C, NaH (1.9 g, 80 mmol) was added and the mixture was allowed to react for 5 min. BnBr (4.75 mL, 40 mmol) was added dropwise. After stirring at room temperature for 3 h, the reaction was quenched by adding MeOH (5 mL) and the reaction mixture was concentrated. The resulting residue was dissolved in ethyl acetate (200 mL) and washed with brine (1×50 mL); the organic phase was dried over Na_2SO_4 and then concentrated. Chromatography of the residue on silica gel using hexane:EtOAc (4:1) afforded compound **22** (2.1 g, 95%). $[\alpha]_D^{22}$ −33.3 (*c* 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.21–7.39 (m, 5H, Bn), 5.38 (d, 1H, *J* 5.2 Hz, H-1), 4.77 (t, 1H, *J* 5.0 Hz, CH$_3$CH$_2$C*H*), 4.58 (d, 1H, *J* 12.0 Hz, Bn), 4.46 (d, 1H, *J* 12.0 Hz, Bn), 4.14 (dq, 1H, *J* 4.2 Hz, 6.7 Hz, H-5), 4.00 (d't', 1H, *J* 3.5 Hz, 5.0 Hz, H-2), 3.61 (d't', 1H, *J* 4.2 Hz, 7.2 Hz, H-4), 2.50 (ddd, 1H, *J* 3.4 Hz, 7.3 Hz, 14.8 Hz, H-3e), 1.68–1.83 (m, 3H, H-3b+CH$_3$C*H*$_2$CH), 1.26 (d, 3H, *J* 6.7 Hz, H-6), 0.98 (t, 3H, *J* 7.6 Hz, C*H*$_3$CH$_2$CH). ^{13}C NMR ($CDCl_3$, from HMQC): δ 127.1–128.3 (Bn), 104.3 (CH$_3$CH$_2$*C*H), 96.8 (C-1), 72.1 (C-2), 72.0 (C-4), 71.3 (PhCH$_2$), 66.2 (C-5), 28.1 (C-3), 26.4 (CH$_3$*C*H$_2$CH), 15.0 (C-6), 8.1 (*C*H$_3$CH$_2$CH). High res. ES-MS: calcd for $C_{16}H_{22}O_4Na^+$: 301.141580; found: 301.14100. Anal. calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.45; H, 7.81.

*3.16. 4-*O*-Benzyl-3,6-dideoxy-α,β-*D*-xylo-hexopyranose **23***

To solution of compound **22** (2 g, 7.2 mmol) in tetrahydrofuran (60 mL), 10% sulfuric acid (18 mL) was added. After being heated at 80°C for 4 h, the mixture was diluted with dichloromethane (300 mL). The organic layer was washed with H_2O (1×30 mL), saturated $NaHCO_3$ (1×50 mL), dried over Na_2SO_4 and evaporated. Chromatography of the resulting residue on silica gel using hexane:EtOAc (3:2) gave compound **23** (1.56 g, 91%). ^{1}H NMR ($CDCl_3$): δ 7.26–7.35 (m, 5H, Bn), 4.69 (d, 1H, *J* 12.1 Hz, Bn), 4.48 ('t', 1H, *J* 7.8 Hz, H-1), 4.45 (d, 1H, *J* 12.1 Hz, Bn), 3.70 (m, 2H, H-2+H-5), 3.39 (m, 1H, H-4), 2.82 (d, 1H, *J* 7.8 Hz, 1-OH), 2.41 (ddd, 1H, *J* 3.0 Hz, 4.9 Hz,13.7 Hz, H-3e), 1.46 (ddd, 1H, *J* 2.8 Hz, 11.8 Hz, 14.1 Hz, H-3b), 1.26 (d, 3H, *J* 6.5 Hz, H-6). 15% α-isomer was found by NMR; selected ^{1}H NMR data: δ 5.24 ('t', 1H, *J* 3.5 Hz, H-1), 4.10 (dq, 1H, *J* 1.7 Hz, 6.5 Hz, H-5), 1.20 (d, 3H, *J* 6.5 Hz, H-6).

High res. ES-MS: calcd for $C_{13}H_{18}O_4Na^+$: 261.11028; found: 261.11073. Anal. calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.13; H, 7.74.

3.17. 1,2-Di-O-acetyl-4-O-benzyl-3,6-dideoxy-α,β-D-xylo-hexopyranose **24**

To solution of compound **23** (1 g, 4.2 mmol) in pyridine (40 mL), acetic anhydride (30 mL) was added. The mixture was stirred at room temperature for 6 h and co-evaporated with toluene (10 mL). Chromatography of the resulting residue on silica gel with hexane:ethyl acetate (3:2) afforded product **24** (1.3 g, 96%). ^{1}H NMR ($CDCl_3$) for α anomer: δ 7.24–7.34 (m, 5H, Bn), 6.22 (d, 1H, *J* 3.4 Hz, H-1), 5.27 (ddd, 1H, *J* 3.4 Hz, 4.8 Hz, 12.3 Hz, H-2), 4.73 (d, 1H, *J* 12.2 Hz, Bn), 4.46 (d, 1H, *J* 12.1 Hz, Bn), 4.01 (dq, 1H, *J* 1.7 Hz, 6.5 Hz, H-5), 3.50 (m, 1H, H-4), 2.32 (m, 1H, H-3a), 2.11 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.90 (m, 1H, H-3b), 1.20 (d, 3H, *J* 6.5 Hz, H-6). ^{1}H NMR ($CDCl_3$) for β anomer: δ 7.24–7.34 (m, 5H, Bn), 5.68 (d, 1H, *J* 8.0 Hz, H-1), 5.06 (ddd, 1H, *J* 4.9 Hz, 8.0 Hz, 12.9 Hz, H-2), 4.73 (d, 1H, *J* 12.2 Hz, Bn), 4.46 (d, 1H, *J* 12.1 Hz, Bn), 3.81 (dq, 1H, *J* 1.7Hz, 6.5 Hz, H-5), 3.42 (m, 1H, H-4), 2.59 (ddd, 1H, *J* 4.3 Hz, 5.0 Hz, 13.7 Hz, H-3e), 2.07 (s, 3H, OAc), 2.02 (s, 3H, OAc), 1.53 (ddd, 1H, *J* 2.4 Hz, 11.2 Hz, 13.8 Hz, H-3a), 1.26 (d, 3H, *J* 6.5 Hz, H-6). α:β anomer ratio is 33:67 by NMR. ^{13}C NMR ($CDCl_3$, from HMQC) for α anomer: δ 128.3–128.1 (m, Bn), 89.5 (C-1, $J_{C1,H1}$ 176.1 Hz), 74.1 (C-4), 70.8 (Bn), 68.6 (C-5), 65.4 (C-2), 26.3 (C-3), 20.6 (2×OAc), 16.0 (C-6). ^{13}C NMR ($CDCl_3$, from HMQC) for β anomer: δ 128.1–128.3 (m, Bn), 93.1 (C-1, $J_{C1,H1}$ 164.6 Hz), 74.4 (C-5), 73.2 (C-4), 70.8 (Bn), 67.0 (C-2), 30.7 (C-3), 20.6 (2×OAc), 16.0 (C-6). High res. ES-MS: calcd for $C_{17}H_{22}O_6Na^+$: 345.13141; found: 345.13171. Anal. calcd for $C_{17}H_{22}O6$: C, 63.34; H, 6.88. Found: C, 63.08; H, 6.99.

3.18. Phenyl 2-O-acetyl-4-O-benzyl-3,6-dideoxy-1-thio-α,β-D-xylo-hexopyranoside **4**

To a mixture of **24** (100 mg, 0.31 mmol), thiophenol (48 μl, 0.47 mmol) and 4 Å molecular sieves in anhydrous CH_2Cl_2 (5 mL) cooled at 4°C under argon, $BF_3 \cdot Et_2O$ (59 μl, 0.47 mmol) was added dropwise. The mixture was stirred at room temperature for 30 min and quenched with Et_3N (1 mL). The solvent was evaporated and the residue was purified by silica gel using hexane:EtOAc (17:3) to give product **4** (107 mg, 93%). ^{1}H NMR ($CDCl_3$) for α anomer: δ 7.20–7.45 (m, 10H, Ar), 5.79 (d, 1H, *J* 5.0 Hz, H-1), 5.36 (d't', 1H, *J* 4.8 Hz, 12.3 Hz, H-2), 4.71 (d, 1H, *J* 12.1 Hz, Bn), 4.47 (d, 1H, *J* 12.1 Hz, Bn), 4.35 (dq, 1H, *J* 1.7 Hz, 6.6 Hz, H-5), 3.54 (m, 1H, H-4), 2.26 (d't', 1H, *J* 3.9 Hz, 13.4 Hz, H-3e), 2.03 (s, 3H, OAc), 1.88 (ddd, 1H, *J* 12.3 Hz, 13.6 Hz, 2.75 Hz, H-3a), 1.20 (d, 3H, *J* 6.6 Hz, H-6). ^{1}H NMR ($CDCl_3$) for β anomer: δ 7.23–7.51 (m, 10H, Ar), 5.06 (ddd, 1H, *J* 4.9 Hz, 10.0 Hz, 11.0 Hz, H-2), 4.71 (d, 1H, *J* 13.0 Hz, Bn), 4.70 (d, 1H, *J* 9.6 Hz, H-1), 4.42 (d, 1H, *J* 12.1 Hz, Bn), 3.66 (dq, 1H, *J* 1.4 Hz, 6.4 Hz, H-5), 3.42 (m, 1H, H-4), 2.59 (ddd, 1H, *J* 3.2 Hz, 4.9 Hz, 13.4 Hz, H-3e), 2.05 (s, 3H, OAc), 1.53 (ddd, 1H, *J* 2.5 Hz, 11.2 Hz, 13.65 Hz, H-3a), 1.29 (d, 3H, *J* 6.6 Hz, H-6). α:β anomer ratio is 24:76 by NMR. High res. ES-MS: calcd for $C_{17}H_{24}O_4SNa^+$: 395.12930; found: 395.12946. Anal. calcd for $C_{17}H_{24}O_4S$: C, 62.93; H, 7.46. Found: C, 63.25; H, 7.58.

3.19. 3,4-O-Benzylidene-(R)-1,2-O-propylidene-6-O-tosyl-α-D-galactopyranose **25**

A solution of compound **14** (1.0 g, 3.24 mmol) in anhydrous pyridine (30 mL) was cooled to 0°C, *p*-toluenesulphonyl chloride (1.3 g, 6.98 mmol) was added in small portions and the reaction was stirred under argon overnight. The mixture was then cooled to 0°C and water (10 mL) was added. After stirring at 0°C for 30 min, the mixture was concentrated. Chromatography of the resulting residue on silica gel with hexane:EtOAc (3:2) afforded compound **25** (1.50 g, quantitative). $[\alpha]_D$ −73.3 (*c* 1.0, MeOH). ^{1}H

NMR ($CDCl_3$): δ 7.78 (d, 2H, *J* 8.4 Hz, Ts), 7.25–7.42 (m, 7H, Ar), 5.68 (s, 1H, PhCH), 5.52 (d, 1H, *J* 5.0 Hz, H-1), 4.81 (t, 1H, *J* 5.1 Hz, CH_3CH_2CH), 4.66 (dd, 1H, *J* 2.7 Hz, 8.1 Hz, H-3), 4.12–4.30 (m, 5H, H-4+H-2+H-5+H-6a+H-6b), 2.38 (s, 3H, OTs), 1.76 (m, 2H, CH_3CH_2CH), 1.01 (t, 3H, *J* 7.5 Hz, CH_3CH_2CH). High res. ES-MS: calcd for $C_{23}H_{26}O_8SNa^+$: 485.12461; found: 485.12468. Anal. calcd for $C_{23}H_{26}O_8S$: C, 59.73; H, 5.67. Found: C, 59.73; H, 5.62.

3.20. 6-O-Acetyl-3-O-benzoyl-4-bromo-4-deoxy-1,2-O-propylidene-α-D-glucopyranose **26**

To the solution containing **15** (57 mg, 0.19 mmol) and barium carbonate (116 mg, 0.59 mmol) in dry CCl_4 (5 mL) was added NBS (49 mg, 0.27 mmol) and the mixture was refluxed for 30 min. After being cooled to room temperature, the mixture was filtered through a thin pad of Celite and the solvent was evaporated. Chromatography of the resulting residue on silica gel with hexane:EtOAc (5:1) afforded compound **26** (51 mg, 79%). $[\alpha]_D^{22}$ −30.0 (*c* 0.3, MeOH). ^{1}H NMR ($CDCl_3$): δ 8.03 (m, 2H, Bz), 7.59 (m, 1H, Bz), 7.45 (m, 2H, Bz), 5.82 ('t', 1H, *J* 3.3 Hz, H-3), 5.67 (d, 1H, *J* 5.1 Hz, H-1), 4.92 (t, 1H, *J* 4.8 Hz, CH_3CH_2CH), 4.45 (dd, 1H, *J* 2.4 Hz, 12.1 Hz, H-6a), 4.36 (ddd, 1H, *J* 2.4 Hz, 4.9 Hz, 10.1 Hz, H-5), 4.31 (dd, 1H, *J* 4.9 Hz, 11.9 Hz, H-6b), 4.16 (dd, 1H, *J* 3.8 Hz, 5.9 Hz, H-2), 4.01 (dd, 1H, *J* 3.1 Hz, 10.1 Hz, H-4), 2.05 (s, 3H, OAc), 1.87 (dq, 2H, *J* 4.9 Hz, 7.5 Hz, CH_3CH_2CH), 1.06 (t, 3H, *J* 7.5 Hz, CH_3CH_2CH). ^{13}C NMR ($CDCl_3$): δ 170.6 (CO), 164.6 (CO), 133.8, 130.0, 129.0, 128.6 (Bz), 105.4 ($CHCH_2CH_3$), 96.9 (C-1), 74.0, 73.2, 70.0 (C-2, 3, 5), 63.5 (C-6), 42.5 (C-4), 26.8 (CH_3CH_2CH), 20.8 (Ac), 8.1 (CH_3CH_2CH). High res. ES-MS: calcd for $C_{18}H_{21}O_7BrNa^+$: 451.03683; found: 451.03686. Anal. calcd for $C_{18}H_{21}BrO_7$: C, 50.36; H, 4.93. Found: C, 50.37; H, 4.72.

3.21. 3-O-Benzoyl-4-O-bromo-4-deoxy-1,2-O-propylidene-6-O-tosyl-α-D-glucopyranose **27**

Compound **25** (100 mg, 0.22 mmol) was reacted with NBS (56 mg, 0.31 mmol) in dry CCl_4 (8 mL) in the presence of barium carbonate (128 mg, 0.65 mmol) as described for **26** to afford compound **27** (100 mg, 86%). $[\alpha]_D^{22}$ −14.2 (*c* 0.4, MeOH). ^{1}H NMR ($CDCl_3$): δ 7.98 (m, 2H, Bz), 7.75 (d, 2H, *J* 7.8 Hz, Ts), 7.58 (m, 1H, Bz), 7.43 (m, 2H, Bz), 7.27 (d, 2H, *J* 7.8 Hz, Ts), 5.74 ('t', 1H, *J* 3.7 Hz, H-3), 5.58 (d, 1H, *J* 5.0 Hz, H-1), 4.86 (t, 1H, *J* 4.9 Hz, CH_3CH_2CH), 4.27–4.33 (m, 3H, H-5+H-6a+H-6b), 4.12 (dd, *J* 3.8 Hz, 5.0 Hz, H-2), 3.95 (dd, 1H, *J* 3.5 Hz, 9.9 Hz, H-4). 2.40, (s, 3H, OTs), 1.79 (dq, 2H, *J* 4.9 Hz, 7.5 Hz, CH_3CH_2CH), 1.00 (t, 3H, *J* 7.5 Hz, CH_3CH_2CH). ^{13}C NMR ($CDCl_3$, from HMQC): δ 128.0–134.0 (Ar), 105.4 ($CHCH_2CH_3$), 96.8 (C-1), 74.0 (C-2), 73.1 (C-3), 70.0 (C-5), 68.5 (C-6), 42.0 (C-4), 26.8 (CH_3CH_2CH), 21.7 (Ts), 8.1 (CH_3CH_2CH). High res. ES-MS: calcd for $C_{23}H_{25}O_8BrNa^+$: 563.03512; found: 563.03579. Anal. calcd for $C_{23}H_{25}BrO_8S$: C, 51.02; H, 4.65. Found: C, 50.94; H, 4.89.

3.22. 3-O-Benzoyl-4-deoxy-1,2-O-propylidene-6-O-tosyl-α-D-xylo-hexopyranose **28**

A mixture of compound **27** (100 mg, 0.18 mmol) and $KHCO_3$ in methanol (30 mL) was hydrogenated in the presence of Pd–C (10%, 50 mg) for 12 h. The catalyst was filtered off and the filtrate was concentrated. Chromatography of the residue on silica gel using hexane:EtOAc (4:1) gave **28** (80 mg, 96%). $[\alpha]_D^{22}$ −5.5 (*c* 0.3, MeOH). ^{1}H NMR ($CDCl_3$): δ 7.98 (m, 2H, Bz), 7.76 (d, 2H, *J* 7.8 Hz, Ts), 7.56 (m, 1H, Bz), 7.43 (m, 2H, Bz), 7.28 (d, 2H, *J* 7.8 Hz, Ts), 5.54 (d, 1H, *J* 5.1 Hz, H-1), 5.44 (d't', 1H, *J* 4.2 Hz, 6.2 Hz, H-3), 4.87 (t, 1H, *J* 4.9 Hz, CH_3CH_2CH), 4.21 (m, 1H, H-5), 4.02–4.07 (m, 3H, H-2+H-6a+H-6b), 2.40 (s, 3H, OTs), 2.18 (ddd, 1H, *J* 4.7 Hz, 6.4 Hz, 14.6 Hz, H-4e), 1.64–1.79 (m, 3H+H-4a+CH_3CH_2CH), 0.99 (t, 3H, *J* 7.5 Hz, CH_3CH_2CH). High res. ES-MS: calcd for $C_{23}H_{26}O_8SK^+$:

501.09855; found: 501.09895. Anal. calcd for $C_{23}H_{26}O_8S$: C, 59.73; H, 5.67. Found: C, 59.77; H, 5.87.

References

1. Davies, D. A. L. *Adv. Carbohydr. Chem. Biochem.* **1960**, *15*, 271–340.
2. Luderitz, O. *Bull. Soc. Chim. Biol.* **1960**, *42*, 1355–1357.
3. Westphal, O.; Luderitz, O. *Angew. Chem.* **1960**, *72*, 881–891.
4. Bundle, D. R. *Top. Current Chem.* **1991**, *154*, 1–37; Bundle, D. R. In *Recognition of Carbohydrate Antigens by Antibody Binding Sites*; Hecht, S., Ed. Carbohydrates. Oxford University Press Inc: Oxford, 1998; pp. 370–440.
5. Jütten, P.; Scharf, H.-D. *J. Carbohydr. Chem.* **1990**, *9*, 675–681.
6. Baer, H. H.; Astles, D. J. *Carbohydr. Res.* **1968**, *126*, 343–347.
7. Pinto, M. B.; Bundle, D. R. *Carbohydr. Res.* **1984**, *133*, 333–338.
8. Classon, B.; Garegg, P. J.; Samuelsson, B. *Can. J. Chem.* **1981**, *59*, 339–343.
9. Zegelaar-Jaarsveld, K.; van der Plas, S.; van der Marel, G. A.; van Boom, J. H. *J. Carbohydr. Chem.* **1996**, *5*, 665–689.
10. Bundle, D. R. *J. Chem. Soc. Perkin Trans. 1* **1979**, 2751–2755.
11. Bock, K.; Lundt, I.; Pedersen, C. *Acta Chem. Scand.* **1981**, *B35*, 155–162.
12. Russell, R. N.; Weigel, T. M.; Han, O.; Liu, H.-W. *Carbohydr. Res.* **1990**, *201*, 95–114.
13. Patroni, J. J.; Stick, R. V. *Aust. J. Chem.* **1978**, *31*, 445–446.
14. Bundle, D. R.; Alibes, R.; Nilar, S.; Otter, A.; Warwas, M.; Zhang, P. *J. Am. Chem. Soc.* **1999**, *120*, 5317–5318.
15. Collins, P. M.; Munasingle, V. R. N.; Oparaeche, N. N. *J. Chem. Soc. Perkin Trans. 1* **1977**, 2423–2428.
16. Gigg, R.; Warrren, C. D. *J. Chem. Soc. (C)* **1968**, 1903–1911.
17. Zagar, C.; Scharf, H.-D. *Carbohydr. Res.* **1993**, *248*, 107–118.
18. Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc. Perkin Trans. 1* **1975**, 1574–1585.
19. Hanessian, S.; Plessas, N. R. *J. Org. Chem.* **1969**, *34*, 1035–1044.
20. Zhang, P.; Bundle, D. R., manuscript in preparation.
21. Gelas, J. *Adv. Carbohydr. Chem. Biochem.* **1981**, *39*, 71–156.
22. Chana, J. S.; Collins, P. M.; Farnia, F.; Peacock, D. J. *J. Chem. Soc. Chem. Commun.* **1988**, 94–96.
23. Bundle, D. R.; Josephson, S. *Can. J. Chem.* **1978**, *56*, 2686–2690.